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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/808,867	03/15/2001	Michael John Bradley Kutryk	1133279-0003	5578

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WHITE & CASE LLP
PATENT DEPARTMENT
1155 AVENUE OF THE AMERICAS
NEW YORK, NY 10036

EXAMINER	
CHATTOPADHYAY, URMI	
ART UNIT	**PAPER NUMBER**
3738	

DATE MAILED: 03/01/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/808,867	KUTRYK ET AL.	
	Examiner	Art Unit	
	Urmi Chattopadhyay	3738	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 September 2004 and 01 December 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-27,29-42,45,46,48,51-55 and 62-76* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☒ Claim(s) *41 and 45* is/are allowed.

6)☒ Claim(s) *1,2,4,5,7-9,18,20-25,27,29-32,38,39,63-65,67,68,70-72 and 74-76* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *15 March 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims withdrawn from consideration are 6,10-17,19,26,33-37,40,42,46,48,51-55,62,66,69 and 73.

DETAILED ACTION

Response to Amendment

1. The amendment filed September 27, 2004 and the Response to Notice of Non-Compliant Amendment filed December 1, 2004 have been entered.

2. Claims 3, 28 and 56-61 have been cancelled, and new claims 62-74 have been added. Claims 6, 10-17, 19, 26, 33-37, 40, 42, 46, 48 and 51-55 remain withdrawn from consideration, and new claims 62, 66, 69 and 73 are also withdrawn from consideration for being drawn to non-elected Species 2c (synthetic material matrix) and Species 2d (naturally occurring material matrix). The claims currently pending are claims 1, 2, 4-27, 29-42, 45, 46, 48, 51-55 and 62-76. The claims being considered for further examination on the merits are 1, 2, 4, 5, 7-9, 18, 20-25, 27, 29-32, 38, 39, 41, 45, 63-65, 67, 68, 70-72 and 74-76.

Specification

3. The abstract of the disclosure is objected to because on line 4, "producing the a medical device" should be changed to --producing the medical device--, by deleting "a". Correction is required. See MPEP § 608.01(b).

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 18, 20, 25, 29, 38, 63, 70 and 74 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

5. Claims 1, 18, 25, 29 and 38 each claim that the antibodies can be "combinations of the antibodies and fragments". While there is support in the specification for antibody fragments used as an alternative to antibodies, there is no support for their combination.

6. Claims 20, 63, 70 and 74 each claim "mixtures thereof" with respect to the Markush listing of elements. While there is support in the specification for the matrix comprising fullerene, synthetic materials and naturally occurring materials as alternatives to each other, there is no support in the specification for the matrix comprising a combination of the fullerene, synthetic materials and naturally occurring materials listed in the claims.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 64, 65, 67, 68, 71, 72, 75 and 76 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

8. Each of claims 64, 65, 67, 68, 71, 72, 75 and 76 is indefinite because they are not commensurate in scope with the claims on which they depend. For example, if the matrix of claim 63 comprises cellulose ester, how does claim 64, which limits the fullerene as ranging

from about C60 to about C100, further limit the cellulose ester matrix? The examiner suggests first limiting the matrix to a fullerene, and then further limiting the fullerene.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. Claims 1, 2, 4, 7, 9, 38, 39, 63 and 64 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dekker et al. (*Improved Adhesion and Proliferation of Human Endothelial Cells on Polyethylene Precoated with Monoclonal Antibodies Directed Against Cell Membrane Antigens and Extracellular Matrix Proteins*, as cited in applicant's IDS) in view of Richmond et al. (USPN 5,310,669 as cited in applicant's IDS).

Dekker et al. discloses a coated medical device and method for treating a mammal for obstruction of a vessel with all the elements of claims 1 and 38, but is silent to the medical device being coated with one or more layers of a matrix. See *Summary* and *Introduction* for treating a mammal for obstruction of a vessel using a medical device (vascular graft) coated with a therapeutically effective amount of at least one type of antibody, which reacts with an endothelial cell antigen. Richmond et al. teaches a substrate coated with a matrix comprising fullerene C60 with an antibody bound thereto (claims 2; see column 5, lines 36-37) in order to facilitate cell attachment and growth, as well as generate highly reactive singlet oxygen, which is useful in the process of studying cell membrane composition e.g., cholesterol content. See

column 3, lines 31-35 and columns 3-4, lines 65-19. It would have been obvious to one of ordinary skill in the art at the time of applicant's invention to look to the teachings of Richmond et al. to modify the medical device and method of Dekker et al. by including to the coating a layer of a matrix comprising a fullerene of about C60 (claims 63 and 64) and attaching the antibodies thereto in order to facilitate cell attachment and growth, as well as generate highly reactive singlet oxygen, which is useful in the process of studying cell membrane composition e.g., cholesterol content.

Claims 4 and 9, see *Summary* for antibody being the monoclonal antibody, $F(ab')_2$ fragments.

Claim 7, see pages 716-717 under *Cell Adhesion and Proliferation* for human endothelial cells.

Claim 39, see line 2 of *Introduction* for vessel being an artery.

11. Claim 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over Dekker et al. and Richmond et al. as applied to claim 1 above, and further in view of Watson et al. (USPN 5,688,486 as cited in last office action).

Dekker et al., as modified by Richmond et al., discloses a coated medical device with all the elements of claim 1, but is silent to the medical device being a stent. Watson et al. teaches a stent coated with a fullerene ranging from about C60 to about C100 in order to provide the stent with singlet oxygen generators. See column 17, lines 55-63. It would have been obvious to one of ordinary skill in the art at the time of applicant's invention to look to the teachings of Watson et al. to coat a stent with the coating of Dekker et al. in order to provide the stent with singlet

oxygen generators. These generators are useful particularly in the areas where stents are required in the process of studying cell membrane composition e.g., cholesterol content.

12. Claim 8 is rejected under 35 U.S.C. 103(a) as being unpatentable over Dekker et al. and Richmond et al. as applied to claim 4 above, and further in view of Asahara et al. (*Isolation of Pututive Progenitor Endothelial Cells for Angiogenesis*, as cited in applicant's IDS).

Dekker et al., as modified by Richmond et al., discloses a coated medical device with all the elements of claim 4, but is silent to the monoclonal antibody reacting with endothelial cell surface antigen CD34, as required by claim 8. Asahara et al. teaches, as disclosed by applicant on page 15 of the specification, using anti-CD34 monoclonal antibodies attached to a solid support in order to capture progenitor endothelial cells that are capable of differentiating into endothelial cells. It would have been obvious to one of ordinary skill in the art at the time of applicant's invention to look to the teachings of Asahara et al. to modify the monoclonal antibody of Dekker et al. so that it reacts with the endothelial cell surface antigen CD34 in order for it to capture progenitor endothelial cells that are capable of differentiating into endothelial cells. This will ultimately increase endothelial cell proliferation and graft patency.

13. Claims 18, 20-22, 24, 25, 27, 67, 70 and 71 are rejected under 35 U.S.C. 103(a) as being unpatentable over Richmond et al. in view of Dekker et al.

Richmond et al. discloses a coating composition for and method of rendering a substrate compatible for *in vivo* attachment and proliferation of cells on the surface with all the elements of claims 18 and 25, but is silent to the antibody reacting with an endothelial cell antigen and the

substrate being a medical device. See abstract and column 5, lines 24-37 for a coating composition that is capable and suitable of being coated to a medical device (the word "for" in claim 18 is intended use language only and the medical device is not a part of the claimed invention), wherein the coating composition comprises a matrix and a therapeutically effective amount of antibodies. The method comprises coating a substrate with a layer of a matrix and binding a therapeutically effective amount of antibodies thereto (claim 27). Dekker et al. teaches coating a medical device (vascular graft) with mixtures of monoclonal antibody $F(ab')_2$ fragments (claims 21 and 24) that react with a human endothelial cell antigen (claim 22) in order to promote adherence of endothelial cells and antibodies directed against the adhesive proteins von Willebrand factor and fibronectin in order to promote endothelial cell proliferation. See *Summary* on page 715 and *Cell Adhesion and Proliferation* on pages 716-717. It would have been obvious to one of ordinary skill in the art at the time of applicant's invention to look to the teachings of Dekker et al. to make the substrate of Richmond et al. a medical device and the antibodies include monoclonal antibody $F(ab')_2$ fragments that react with a human endothelial cell antigen in order to promote adherence of endothelial cells and antibodies directed against the adhesive proteins von Willebrand factor and fibronectin in order to promote endothelial cell proliferation. A medical device coated with the coating composition, which includes both types of antibodies, will be rendered compatible for *in vivo* attachment and proliferation of cells on the surface thereof.

Claims 20, 67, 70 and 71, see column 3, lines 8-14 for the matrix comprising fullerene within the required range.

14. Claim 23 is rejected under 35 U.S.C. 103(a) as being unpatentable over Richmond et al. and Dekker et al. as applied to claim 21 above, and further in view of Asahara et al.

Richmond et al., as modified by Dekker et al., discloses a composition with all the elements of claim 21, but is silent to the monoclonal antibody reacting with endothelial cell surface antigen CD34, as required by claim 23. Asahara et al. teaches, as disclosed by applicant on page 15 of the specification, using anti-CD34 monoclonal antibodies attached to a solid support in order to capture progenitor endothelial cells that are capable of differentiating into endothelial cells. It would have been obvious to one of ordinary skill in the art at the time of applicant's invention to look to the teachings of Asahara et al. to modify the monoclonal antibody of Dekker et al. so that it reacts with the endothelial cell surface antigen CD34 in order for it to capture progenitor endothelial cells that are capable of differentiating into endothelial cells. This will ultimately increase endothelial cell proliferation and graft patency.

15. Claims 29-32, 74 and 75 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dekker et al. in view of Richmond et al. and Bos et al. (*Small-Diameter Vascular Graft Prosthesis: Current Status*, as cited in applicant's IDS).

Dekker et al. discloses a method for treating a mammal with obstructed arteries with all the elements of claim 29, but is silent to the method specifically treating for atherosclerosis and the medical device being coated with one or more layers of a matrix. See *Summary* and *Introduction* for treating a mammal for obstruction of a vessel using a medical device (vascular graft) coated with a therapeutically effective amount of at least one type of antibody, which reacts with an endothelial cell antigen. Richmond et al. teaches a substrate coated with a matrix

comprising fullerene C60 with an antibody attached thereto in order to facilitate cell attachment and growth, as well as generate highly reactive singlet oxygen, which is useful in the process of studying cell membrane composition e.g., cholesterol content. See column 3, lines 31-35 and columns 3-4, lines 65-19. It would have been obvious to one of ordinary skill in the art at the time of applicant's invention to look to the teachings of Richmond et al. to modify the method of Dekker et al. by including to the medical device antibody coating a layer of matrix comprising a fullerene of about C60 (claims 74 and 75) in order to facilitate cell attachment and growth, as well as generate highly reactive singlet oxygen, which is useful in the process of studying cell membrane composition e.g., cholesterol content. Bos et al. teaches that it is old and well known in the art to treat mammals for atherosclerosis with grafts under *Introduction* (first paragraph). It would have been obvious, therefore, to one of ordinary skill in the art to use the graft of Dekker et al. to treat atherosclerosis, specifically in the coronary artery (claim 31), because it is customary to do so.

Claims 30 and 32, see *Summary* of Dekker et al. for the antibody being monoclonal antibody $F(ab')_2$ fragments.

Double Patenting

16. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground

provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

17. Claims 1, 2, 4, 5, 7-9, 29-32, 38, 39, 63, 64, 74 and 75 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3, 7-15, 25-33, 35-39, 42-47, 49 and 50 of copending Application No. 10/360,567. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the current application include all of the limitations of those of the copending application and are broader in scope.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Allowable Subject Matter

18. Claims 41 and 45 are allowed.

19. Claims 65, 68, 72 and 76 would be allowable if rewritten to overcome the rejection(s) under 35 U.S.C. 112, 2nd paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

Response to Arguments

20. Applicant's arguments filed 1/16/04 have been fully considered but they are not persuasive.

21. Applicant's arguments are directed against the Dekker et al. reference, which was used in combination with at least one other reference in each of the §103 rejections. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., proliferation of circulating cells on a polyethylene layer with surface-adsorbed monoclonal antibodies directed against endothelial cell membrane proteins) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Claims 1, 29 and 38 do not even mention proliferation. Claim 18 and 25 do not require that the cells proliferate with the monoclonal antibodies directed against endothelial cell membrane proteins. Rather, they only require that the coating composition and method render a medical device compatible for proliferation of cells on the surface thereof. The antibodies directed against the adhesive proteins von Willebrand factor and fibronectin of Dekker et al. are causing the proliferation.

22. In response to applicant's argument that in contrast to the claimed invention which achieves *in vivo* selection and adhesion of cells circulating in the bloodstream, the disclosure of Dekker et al. is limited to the *in vitro* coverage of vascular grafts with seeded endothelial cells, a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. See *In re Casey*, 370 F.2d 576, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 312 F.2d 937, 939, 136 USPQ 458, 459 (CCPA 1963).

In vivo attachment of cells is only mentioned in claims 18 and 25. If the coating composition of Dekker et al. was to be applied to a medical device, which was then implanted in the body, the medical device would indeed be rendered compatible for *in vivo* attachment of cells on the surface thereof. It is not required that Dekker et al., Richmond et al. or Asahara et al. disclose *in vivo* proliferation, but only that their combinations (as set forth in the above rejections) produce a structure that allows for *in vivo* attachment of cells, which they do.

23. Applicant argues that in contrast to the use of two categories of antibodies for attachment and proliferation of cells disclosed by Dekker et al., the claimed coated device and coating composition advantageously provide a surface coated with only one class of antibodies which captures circulating cells which then become attached to the surface and proliferation to form a surface that decreases and/or prevents restenosis and thrombosis. None of the claims require "only one class of antibodies". Each of the independent claims uses "comprising" and/or "comprises", which renders the claimed invention open to structural limitations not explicitly recited in the claims. Therefore, applicant's claimed invention is open to the inclusion of antibodies directed against the adhesive proteins von Willebrand factor and fibronectin for cell proliferation.

Conclusion

24. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Urmi Chattopadhyay whose telephone number is (571) 272-4748. The examiner can normally be reached on Tuesday-Thursday 10:00am - 6:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Corrine McDermott can be reached on (571) 272-4754. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Urmi Chattopadhyay
Art Unit 3738

David J. Isabella
Primary Examiner